2023 Summer Student Poster Day
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Session #1

Maisa Samiee
Natasha Kaprelova
Ariel Qi
Emily Simpson
Venessa Thorsen
Rory Trevorrow
Amrith Vincent
Thumri Waliwitiya
Maisa Samiee
Undergraduate Student, University of British Columbia

Supervisor: Simon Massey

Monitoring Antagonism of Neuromuscular Blockade: BCWH Current Practice Compared to the American Society of Anesthesiologists 2023 Practice Guideline: a retrospective clinical audit

Abstract & Poster - https://bcchr.ca/posterday
Natasha Kaprelova
Master’s Student, University of British Columbia

Supervisor: Chinten James Lim

Investigating MYC Amplification in IL-6/JAK/STAT3-Mediated Treatment Resistance in Group 3 Medulloblastoma

Abstract & Poster - https://bcchr.ca/posterday
Investigating c-Myc Amplification in IL-6/JAK/STAT3-Mediated Chemoresistance in Group 3 Medulloblastoma

Natasha Karpelova1,3, Chinten James Lim2,3
1Dept of Medicine, 2Dept of Pediatrics, University of British Columbia
3Michael Cuccione Childhood Cancer Research Program, BC Children’s Hospital Research Institute, Vancouver, B.C., Canada

Background and Introduction

Medulloblastoma (MB) is the most common malignant brain tumour in children, accounting for 25% of all childhood brain tumours. MB was once believed to be a single disease entity, but transcriptional profiling studies have revealed existence of 4 subgroups: WNT, SHH, Group 3 and Group 4. Each subgroup exhibits distinctly different biology, prognosis and risk implications.

Group 3 MB is the most aggressive subgroup and has the worst prognosis. The lack of effective therapeutic treatments for this subgroup due to a limited understanding of its molecular pathways necessitates further studies to understand the mechanisms of tumor progression and aggressive tumor behavior.

Hypothesis/Aims/Experimental Approach

The IL-6/JAK/STAT3 signaling pathway mediates the acquired chemoresistance in the most aggressive subtype of MB (Group 3) is dependent on c-Myc amplification and function.

Aim 1: Establish the Requirement of MYC in IL-6/JAK/STAT3 Mediated Chemoresistance

Aim 2: Assess if Combination of MYC Inhibitors with Vincristine will Overcome Chemoresistance

Modeling Chemoresistance

Exogenous IL-6 conditioning promotes drug resistance in Group 3 MB cell lines

Preliminary Findings

IL-6/JAK/STAT3 Signaling Pathway Drives Chemoresistance in Group 3 Medulloblastoma

Exogenous IL-6 conditioning results in increased levels of c-Myc

Anticipated Results

• Preliminary data suggests that amplification of c-Myc in Group 3 Medulloblastoma is dependent on IL-6 cytokine levels being secreted in the tumor microenvironment.
• I anticipate that following knockdown of IL-6/JAK/STAT3 signaling components (IL-6R, gp130 and STAT3), cells conditioned with IL-6 cytokine will still reveal upregulated expression of c-Myc levels relative to basal conditions. This discovery can reveal a significant finding in that IL-6 cytokine can signal through non-IL6R, proposing a novel signaling mechanism in the IL-6/JAK/STAT3 signaling pathway.
• I anticipate that CRISPR-mediated knockout of c-Myc will decrease Group 3 MB cell lines’ chemoresistance to vincristine, highlighting c-Myc as a crucial component in driving drug resistance.

Significance and Future Directions

The current proposal addresses the molecular mechanisms of IL-6/JAK/STAT3 signaling uniquely implicated in acquired drug resistance in c-Myc-amplified Group 3 MB cells. The expected research findings will identify molecular therapeutic targets that can be used to inform development of novel strategies to combat pediatric brain tumors with the worst prognosis and offer novel pre-clinical insight into efficacy for targeting c-Myc, paving the way for the development of the first effective treatment that targets c-Myc.

References

• Lippitz et al. Oncology 5. 10.1080/2162402X.2015.1093722.
• Schwalbe et al. Cell Death Dis 17, 1883, 10.1038/cddis.2016.193.
Ariel Qi
Medical Student, Queen’s University

Supervisor: S. Evelyn Stewart

Exploring Family Factors in Pediatric Obsessive-Compulsive Disorder and Psychiatric Outpatient Controls

Abstract & Poster - https://bcchr.ca/posterday
Exploring Family Factors in Pediatric Obsessive-Compulsive Disorder and Psychiatric Outpatient Controls

Ariel (Ruo Chen) Qi, John R. Best, Gordon Andjelic, Anna MacLeIan, Boyee Lin, Cynthia Lu, S. Evelyn Stewart
Faculty of Medicine, Queen's University; British Columbia Children's Hospital Research Institute; Department of Psychiatry, University of British Columbia; British Columbia Mental Health and Substance Use Research Institute

Background

Youth psychiatric illness can place a heavy burden on the family. In turn, the family environment could impact prognosis and treatment adherence in the youth. Thus, consideration of family factors is critical in the context of pediatric psychiatric illness.

Family functioning impairment has been well characterized in pediatric obsessive-compulsive disorder (OCD), with profound impacts on family routines, socio-occupational factors and emotional responses. In pediatric OCD, poor parental tolerance of child's distress (PTCD) and accommodation behaviors are associated with increased symptom severity and treatment resistance.

Proposed Study

Objectives:
1. Compare various aspects of family functioning impairment and PTCD in OCD compare to that experienced in families coping with other youth psychiatric conditions.
2. Explore how patient/family characteristics influence the degree of disease-related family functioning impairment and PTCD

Rationale:
There remains a need to characterize how family functioning impairment and PTCD in OCD compare to that experienced in families coping with other youth psychiatric conditions.

Methodology

Data
- Family Input Tool at BC Children's Hospital (n=4009, years 2019-2023)
- 6 outpatient psychiatry clinics
- OCD registry of the Provincial OCD Program (n=398, years 2011-2020)

Predictors of Interest:
- Patient demographics, psychiatric illness (OCD vs. non-OCD), and medical history
- Patient’s family environment
- Family’s medical history (psychiatric diagnoses in particular)

Outcome Measures:
- 21-item Family Functioning Impairment Scale (modified from the validated OCD Family Functioning Scale)
- 3-item PTCD Scale (modified from the validated Distress Tolerance Scale)

Statistical analysis:
- Multivariable linear regression models, whereby the family-related outcome score is regressed on clinical predictors and covariates

This project has been approved by the UBC Research Ethics Board.

Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-OCD, N=3,748</th>
<th>OCD, N=652</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Input Tool</td>
<td>3,748 (100%)</td>
<td>254 (39%)</td>
</tr>
<tr>
<td>OCD registry</td>
<td>0 (0%)</td>
<td>398 (63%)</td>
</tr>
<tr>
<td>Age (Missing)</td>
<td>1.46</td>
<td>1.46</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>967 (41%)</td>
<td>246 (55%)</td>
</tr>
<tr>
<td>Male</td>
<td>1,283 (56%)</td>
<td>196 (44%)</td>
</tr>
<tr>
<td>Other</td>
<td>119 (5.1%)</td>
<td>11 (2.4%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-White</td>
<td>318 (18%)</td>
<td>69 (14%)</td>
</tr>
<tr>
<td>White</td>
<td>1,700 (79%)</td>
<td>397 (82%)</td>
</tr>
<tr>
<td>Other/Don’t know</td>
<td>76 (3.5%)</td>
<td>19 (3.3%)</td>
</tr>
<tr>
<td>Highest Parental Education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than university degree</td>
<td>783 (36%)</td>
<td>150 (30%)</td>
</tr>
<tr>
<td>University degree or greater</td>
<td>1,352 (62%)</td>
<td>337 (68%)</td>
</tr>
<tr>
<td>Other/Not sure</td>
<td>44 (2.0%)</td>
<td>5 (1.0%)</td>
</tr>
<tr>
<td>Parental Marital Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married/Common-law</td>
<td>1,366 (70%)</td>
<td>393 (79%)</td>
</tr>
<tr>
<td>Separated/Divorced</td>
<td>434 (20%)</td>
<td>82 (16%)</td>
</tr>
<tr>
<td>Other/Not sure</td>
<td>210 (9.6%)</td>
<td>22 (4.4%)</td>
</tr>
</tbody>
</table>

Table 1: Participant characteristics breakdown based on sample source, age, gender, ethnicity, parental education status and marital status

Significance

This project will characterize and compare family functioning impairment and PTCD in non-OCD youth psychiatric disorders in relation to OCD.

Results will help identify populations of patients who experience greater family dysfunction.

Our findings could also inform targeted interventions, treatment strategies and social supports that are catered to the unique circumstances of the youth patients and their families.

References


Acknowledgements
Sleep quality in children and youth with type 1 diabetes: a validation study utilizing commercial activity trackers
BACKGROUND

• Over 2,500 children and youth in BC live with diabetes1

• Children with type 1 diabetes (T1D) are particularly vulnerable to experiencing disturbed sleep and inadequate sleep has been linked to reduced executive functioning and quality of life2

OBJECTIVE

• To establish validity of a consumer wearable, the Fitbit Charge 5, for the assessment of sleep behaviours in children and youth with T1D

METHODS

• An observational longitudinal study assessing sleep via commercial activity trackers and sleep logs over a 7-day period

  • Surveys: Parent/Guardians completed Demographic Questionnaire and Sleep Disturbance Scale for Children (SDSC)3
  
  • Fitbit: REDCap extracted min-by-min Fitbit sleep data via a custom written API
  
  • Sleep Logs: Participants received an SMS message each morning with a survey link to capture information on bed/wake time, sleep quality, and diabetes indicators
  
  • Opt-in: Some provided access to sleep-relevant CGM data to analyze relationships between sleep data and clinical outcomes

  • Agreement in Fitbit and sleep log data was assessed via intra-class correlation coefficients and Bland Altman Analyses

RESULTS

Table 1. Sample Characteristics

<table>
<thead>
<tr>
<th>n</th>
<th>Age (yrs ± SD)</th>
<th>% Girls</th>
<th>Time Since Diagnosis (yrs ± SD)</th>
<th>A1C (% ± SD)</th>
<th>% CGM</th>
<th>% Insulin Pump</th>
<th>SDSC Total Score (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>10.74 ± 3.19</td>
<td>38%</td>
<td>5.67 ± 4.44</td>
<td>6.96 ± 0.73</td>
<td>88%</td>
<td>75%</td>
<td>48.63 ± 8.63</td>
</tr>
</tbody>
</table>

CGM – Continuous Glucose Monitor; SDSC – Sleep Disturbance Scale for Children

Table 2. Sleep metrics and agreement between Fitbit and sleep log

<table>
<thead>
<tr>
<th>Persons (n)</th>
<th>Person-Days (m)</th>
<th>Duration/Time of Night (hh:mm)</th>
<th>ICC</th>
<th>Bias (LoA) in Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>46</td>
<td>9:36 ± 1:14</td>
<td>0.57**</td>
<td>-36 (120 to 192)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9:01 ± 1:12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wake Time</td>
<td>7:44 AM ± 1:08</td>
<td>7:22 AM ± 1:13</td>
<td>0.60***</td>
<td>-23 (-97 to 142)</td>
</tr>
<tr>
<td>Bed Time</td>
<td>10:06 PM ± 1:21</td>
<td>10:14 PM ± 1:19</td>
<td>0.72***</td>
<td>-8 (-126 to 110)</td>
</tr>
</tbody>
</table>

*LoA = Limits of Agreement

CONCLUSIONS

• There was a moderately strong positive association between self-reported sleep quality and Fitbit-derived sleep efficiency score

• There was significant but poor (duration) to moderate (bed and wake time) agreement between the Fitbit and sleep logs

• Based on preliminary analysis, I believe there is a use for the Fitbit Charge 5 in sleep research for children and youth with T1D

ACKNOWLEDGEMENTS

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REFERENCES


Emily Simpson1,2, Ty Sideroff1,3, Nick Wall1, Elizabeth Keys4, Quevie Reinz Abalde4, Calli Davidson1,3, Simran Gill1,5, Holly Buhler6, Trent Smith6, Deanne Taylor6, Christine Voss1,7

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Knowledge to Action: Developing a Knowledge Translation Strategy to Improve Management of Familial Hypercholesterolemia in British Columbia

Abstract & Poster - https://bcchr.ca/posterday
Developing a Knowledge Translation Strategy to Improve Management of Familial Hypercholesterolemia in British Columbia

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²Department of Occupational Science & Occupational Therapy, University of British Columbia
³School of Population and Public Health, University of British Columbia

BACKGROUND

Children with untreated cholesterol disorders such as Familial Hypercholesterolemia (FH) have an increased risk of heart attack and stroke in early adulthood.¹,² Lack of clinical practice guidelines for pediatric FH were cited by physicians as a major barrier to management.²

METHODS

Knowledge Translation Intervention
- Case-based learning
- Interactive sessions with polling activities and discussions
- Synchronous/asynchronous delivery
- Based on 2022 CCS guidelines
- Led by pediatric cardiologists
- CPD accredited

One-month Follow-up
- Assess learning, familiarity and confidence managing pediatric dyslipidemias based on responses to patient vignettes
- Self-reported behaviour change
- Satisfaction with the intervention and feedback

OBJECTIVE/AIM

To increase screening and management of pediatric dyslipidemias amongst family physicians and pediatricians in British Columbia.

INCLUSION CRITERIA

Participants who:
- Are licensed family physicians or pediatricians in British Columbia (including academic-based, community-based and subspecialty)
- Routinely care for patients between the ages of 9-11
- Consider themselves to be the primary caregiver for some and/or all of their patients

EXPECTED OUTCOMES

- Anticipated sample size of 50-100+ doctors across BC
- Increased confidence, learning and self-reported behaviour change after 1 month
- Increases in screening, diagnosis and treatment of dyslipidemias across BC at 1 year post-webinar

REFERENCES


ACKNOWLEDGEMENTS

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Supervisor: Lise Leveille

Perioperative Management of Juvenile Idiopathic Arthritis (JIA) in Anterior Cruciate Ligament (ACL) Reconstruction

Abstract & Poster - https://bcchr.ca/posterday
Background
Juvenile idiopathic arthritis (JIA) refers to a group of conditions of unknown etiology characterized by joint inflammation presenting prior to 16 years of age and persisting for a minimum of 6 weeks duration. JIA may co-occur with other musculoskeletal injuries and diseases, including anterior cruciate ligament (ACL) rupture. In the paediatric population, early operative management of ACL rupture is associated with a decreased likelihood of joint instability, pathological laxity, and symptomatic meniscal tears compared to non-operative management. In children with JIA, the inherent inflammatory environment of the joint may interfere with post-surgical healing and rehabilitation. However, medication used to manage JIA, such as corticosteroids, NSAIDs, biological DMARDs, and synthetic DMARDs may also increase complication risk. As such, further understanding of the optimal management of disease activity in the perioperative period may be critical to improve surgical outcomes and reduce complication rates following paediatric ACL reconstruction.

Objective
The aim of the present study is to determine best practices for the medical management of JIA during the perioperative period of paediatric ACL reconstruction.

Methods
Existing literature on the management of inflammatory arthritis in the perioperative period was gathered through a structured search of MEDLINE, Embase and CINAHL databases. A combination of keywords and subject headings related to juvenile arthritis, ACL reconstruction, orthopaedic procedures, and perioperative care was used to identify articles with potential relevance. In addition, recent cases of ACL reconstruction in patients diagnosed with JIA will be identified from the health records of BC Children’s Hospital and reviewed for trends in JIA management and surgical outcomes.

Preliminary Results
A total of 1688 references were identified by the initial search, with 1296 references remaining after the removal of duplicates. Title and abstract screening by a single reviewer yielded 351 articles for full-text review. Progress to date has identified 48 studies mentioning the perioperative medical management of JIA and/or the complication risk associated with unmanaged JIA in the perioperative window.

Implications
The findings of this study may serve to guide the management of DMARDs, corticosteroids, and other antirheumatic medications during the perioperative period of paediatric ACL reconstruction. Optimal medical management of JIA in the perioperative window could serve to improve surgical outcomes and reduce complication rates for paediatric ACL reconstruction and other orthopaedic procedures.
Amrith Vincent
Medical Student, Royal College of Surgeons in Ireland

Supervisor: Linlea Armstrong

Path to Progress: Managing Leukemia
Predisposition in Pediatric Patients

Abstract & Poster - https://bcchr.ca/posterday
Path to Progress: Managing Leukemia Predisposition in Pediatric Patients

Background
Leukemia is one of the most common childhood cancers, accounting for 29%. Most pediatric leukemia patients have sporadic somatic variants. Some are at risk due to germline variants. It is estimated that nearly 10% of pediatric cancer patients have a germline variant in a cancer predisposition gene. The leukemia variants affect key regulatory processes at the cellular level, such as DNA repair and genomic stability. The most common leukemia predisposition genes are somatically changed in other cancers (e.g., TP53, RUNX1, IKZF1, and ETV6).

Objective
Our goal is to create a comprehensive care pathway that allows clinicians to identify and provide personalized care plans to patients and families with a pediatric leukemia predisposition syndrome. Recognizing predisposition syndromes are important due to differences in clinical management, the need for genetic counseling and for hematopoietic stem cell donor selection.

Methods
A comprehensive literature search was performed using the PubMed database and internet search engines. Search terms included "leukemia," "pediatric," "predisposition," and "therapeutics." Exclusion criteria included adult only predisposition syndromes.

Conclusions
The care pathway will be a valuable resource for clinicians navigating the complex landscape of pediatric leukemia predisposition syndromes, providing the blueprint for the creation of personalized care plans throughout the patient’s journey.

Care pathway

Recognition
- Clinical features: age, family history of conditions such as bone marrow failure, aplastic anemia etc.
- Physical exam findings could include features such as variations in growth, skeletal malformations and skin/mucosal/hair changes

Cancer Predisposition Syndrome Diagnostic Assessment
- Review of historic CBC’s, Hemoglobin electrophoresis
- Bone marrow biopsy, with morphology, cytogenetic analysis, and molecular testing
- Trypsinogen, pancreatic isoamylase
- Erythrocyte ADA
- Liver transaminases
- Immunoglobulin levels
- Somatic and / or germline genetic testing
  i. Metaphase cytogenetic analysis
  ii. Chromosomal microarray
  iii. Single nucleotide polymorphism array
  iv. Fluorescent in situ hybridization (FISH)
  v. Next-generation sequencing

Management of the Cancer Predisposition Syndrome
- Genetic counselling
- Specific management varies between specific syndromes
  • Treatment
  • Diagnostic Imaging
  • Surveillance
- Management for the family

Transition to Adult Care
- Address needs and knowledge gaps of patient and families through transition tools
- Early start on education of patient
- Communication between healthcare providers
- Multidisciplinary conferences

Bone marrow aspirate showing acute megakaryoblastic leukemia associated with Down syndrome (50x)

Acknowledgements
Thank you to the generosity of donors through BC Children’s Hospital Foundation.
Thumri Waliwitiya
Medical Student, University of British Columbia

Supervisor: Tim Oberlander

Game Based Intervention for Improving Executive Function in Children with Congenital/Acquired Heart Disease

Abstract & Poster - https://bcchr.ca/posterday
Game Based Intervention for Improving Executive Function in Children with Congenital/Acquired Heart Disease

Thumri Waliwitiya1, Sarah M. Hutchison1, Yaewon Kim2, Buse Bedir2, John Sheehan2, Astrid De Souza1, Kathryn R. Armstrong1, Sarah J. Macoun2, and Tim F. Oberlander3

1University of British Columbia and BC Children’s Hospital 2University of Victoria

Introduction

Many children with congenital heart disease (CHD) are at risk of experiencing executive function (EF) difficulties. EF skills help one to control actions, thoughts, and emotions, as well as to plan, organize, and execute complex tasks. They are critical for academic and psychosocial success, self-care, and successful transition from the pediatric to adult medical system. Children with CHD may have problems with working memory, inhibition, and shifting in performance-based tasks.

Recently there has been interest in delivering online cognitive interventions. There is mounting evidence that computerized attention/EF training can be effective for developmentally and neurologically diverse populations if delivered appropriately.

Study Objectives

1. To work with stakeholders (CHD patients and team) to administer the EF intervention.
2. To determine the feasibility of using this intervention, the level of engagement, and satisfaction of CHD patients, their family, and their CHD team with the EF intervention.
3. To measure EF, and brain function in children with CHD. To measure quality of life (QoL) of children and their families pre- and post-implementation of the EF intervention.

“The video game is a treatment program that kids will stick with long enough to make it effective and doesn’t require a clinical expert to deliver it”
- Dr. Sarah Macoun

Significance

- As most children with CHD survive into adulthood, there has been a shift to optimize long-term outcomes in these patients.
- Our study aims to improve EF in children with CHD using innovative game-based intervention which has shown to be effective in other clinical populations with poor EF skills.
- Improving EF and academic skills may be beneficial for long-term health outcomes and QoL in children with CHD.

Methods

Recruitment and Pre-Training Assessment

- Letter of invitation sent to all eligible participants in the BCCH Heart Center
- Pre-training assessment at BCCH, Online training for parents on intervention delivery
- Outcomes measured by: Verbal intelligence, Nonverbal intelligence, Verbal and spatial working memory, Cognitive flexibility, Spatial working memory, Sustained attention

Game Play

- Participants play Dino Island for 6 weeks
- 3 40-60 min sessions/week

Post-Training Assessment

- Outcome assessment
- Collection of feedback from participating families on their experience

“You go from this really simple switching where the game just tells them what to do, to having to monitor and figure it out themselves, which gets into more of the executive functioning and higher order aspects”
- Dr. Sarah Macoun

T. Waliwitiya was supported during this work as it was generously funded by grants from the BC Children’s Hospital Research Institute.

This work was conducted out of Vancouver, Canada on the traditional, ancestral, and unceded territories of the xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Sel Híl Hwitulh (Tsleil-Waututh) Nations.